Exhibit 4

File Name:

ANAVEX 2-73 (Blarcamesine) AVATAR Phase 3 Trial met Primary and Secondary Endpoints for the Treatment of Adult Patients with Rett Syndrome
February 1, 2022

LEGEND:

[UI]: Unintelligible
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MANAGEMENT DISCUSSION SECTION

Clint Tomlinson
Good morning and welcome, everyone. Welcome to the ANAVEX Life Sciences AVATAR ANAVEX 2-73 Phase 3. Top-Line Data Conference Call. My name is Clint Tomlinson, and I will be your host for today's call. At this time, all participants are in a listen-only mode. Later, we will conduct a question-and-answer session. During this session, if you would like to ask a question, please use the Q&A box or raise your hand.

Please note this conference is being recorded. The call will be available for replay on ANAVEX's website at www.anavex.com.

With us today is Dr. Christopher Missling, President and Chief Executive Officer; and Dr. Ed Hammond, Chief Medical Officer; and Walter E. Kaufmann, Chief Scientific Officer.

Before we begin, please note that during this conference call, the company will make some projections and forward-looking statements. These statements are only predictions based on current information and expectations and involve a number of risks and uncertainties. We encourage you to review the company filings with the SEC. This includes, without limitation, the company's Forms 10-K and 10-Q, which identify specific factors that may cause actual results or events to differ materially from those described in these forward-looking statements. These factors may include, without limitation, risks inherent in the development and/or commercialization of potential products, uncertainty in the results of clinical trials or regulatory approvals, need and ability to obtain future capital, and maintenance of intellectual property rights.

And with that, I would like to turn the call over to Dr. Missling.

Christopher U. Missling
Thank you, Clint. We appreciate everyone joining us on today's conference call to review our reported AVATAR Phase 3 ANAVEX 2-73 study in Rett syndrome top-line data results. In summary, we are very pleased to report the positive results from the Phase 3 clinical trial of the ANAVEX 2-73 AVATAR in adult patients with Rett syndrome.

The study reached primary and secondary endpoints of efficacy, safety, respectively. The study reached primary and all secondary efficacy and safety endpoints, which were all pre-specified, with consistent improvements in RSBQ AUC p value of 0.037, ADAMS p value of 0.010, and CGI-I p value of 0.037 response. Efficacy endpoints demonstrated statistically significant and clinically meaningful reductions in Rett syndrome symptoms, with related changes in potential biomarkers GABA and L-AAA of disease pathology. The key milestones were met to advance now for regulatory approval pathway for adult patients with Rett syndrome.

I'd like now to share the presentation, which goes along with the data today. First, I'd like to share with you what is Rett syndrome. Rett syndrome is a devastating neurodevelopmental disease in girls and adult girls with both movement impairments and cognitive impairments. This is not inherited, and it's a spontaneous mutation of one gene called the MECP2 gene. It occurs almost exclusively in girls, and boys die right away or before birth. It leads to severe impairments affecting nearly every aspect of the child's life. The impairment includes the ability to speak, the ability to walk, eat and even breathe easily.

The hallmarks of Rett syndrome is near constant, repetitive head movements while awake. It occurs worldwide and approximately 1 in every 10,000 to 15,000 live female births, and the population of patients with Rett syndrome is estimated to be approximately 11,000

patients in the US and similar numbers in Europe and Japan as well. So three times that number in the developing countries at least. And there's not currently any cure for Rett syndrome.

The mechanism of action of ANAVEX 2-73 is now known to be very upstream. We understand now that the activation of SIGMAR1, which is the mode of action of ANAVEX 2-73, prevents cellular stress before and after gene transcription. And that might play out very handily in a genetically caused disease like Rett syndrome. And we see that SIGMAR1 is able to prevent and protect chromatin remodeling from worsening, as well as it prevents the RNA, which is toxic, which is caused by a mutated gene, to be expressed into a protein which is toxic as well or not healthy, to guardrail this and to prevent it to express it in a toxic protein, so only healthy proteins are expressed.

As an overview of the Rett syndrome program, we have now almost completed the entire program. We completed the US Phase 2 study, and we just announced the completion of the Phase 3 AVATAR adult Rett syndrome study. And ongoing is still the EXCELLENCE study, which includes patients aged 5 to 17, which is a pediatric clinical study in Rett syndrome under the ANAVEX 2-73 Rett syndrome program.

I'd also like to mention that we received the fast track designation, orphan drug designation, as well as orphan drug in rare pediatric disease designation. So with that, we now have one pivotal study, Phase 3 in adult Rett syndrome, one Phase 2 study which could be a supportive efficacy study in Rett syndrome, and we have extensive database and tolerability data of ANAVEX 2-73 from various other trials as well, which complete the safety package.

Let me share with you the design of the study. It was a relatively small study, 33 patients in total. 20 were randomized to active arm, who received up to 30 milligram once-daily liquid formulation in a convenient formulation, and 13 patients received placebo. They were measured along seven weeks with a data point also captured in addition to baseline at week four. All patients are now eligible to an extension study which lasts 48 weeks.

As a primary endpoint, which was pre-specified, the RSBQ AUC response in safety was measured. In the secondary endpoint, which were efficacy endpoints as well, the emotional behavior, ADAMS response, was measured, as well as the clinical global impression of improvement response, CGI-I. We also had several other exploratory endpoints thereafter, and I'd like to highlight, especially today the Child Health Questionnaire-Patient (sic) [Parent] Form 50, as well as the seizure diary, which we address later today in the slideshow. The other endpoints like biomarker SIGMAR1 are still being assessed, as well as Mrna, and are not available yet for the top-line data but will be available later at some point in time, which we will report.

Let me share with you the baseline characteristics. You see across the two arms a very relatively well-balanced baseline in regard to the age, weight, and the severity of the disease. You could even say that the ANAVEX arm had a slightly higher marked ill baseline compared to the placebo. But overall, it's a relatively balanced picture of the

patients' respective features. I'd also like to point out that the seizure medication was higher than compared to the RS-001 US study, with N average of 82%. So these patients were on average more severely impaired than the study we reported from the US RS-001 study.

So let me give you some background, however, about the endpoints, the primary endpoint, which is very important. It has been demonstrated that statistically significance, and it is required for a successful Phase 3 study, is not alone sufficient for approving a drug. It's also required that the outcome of the effect of the patients is clinically meaningful for the individual patient, and that can be measurable, assessed.

And for that reason, to pick the right endpoint is very important. As we know now, and we knew when we started the trial, the RSBQ is not the most suited standalone caregiver endpoint or outcome assessment for Rett syndrome. It had been shown and recently published that it could lead to either type 1 or type 2 error.

The FDA hence recommended, and it's also provided in the guidelines from the FDA and recommended specifically in these cases because you don't have many choices of endpoints to pick from, which have been validated for rare diseases like Rett syndrome, to use instead the RSBQ with an anchor. That's called anchor-based responder method, which links the score from one clinical outcome assessment, the RSBQ in this case, with scores from a simple reference anchor, which is the outcome assessment with a clinically meaningful threshold, which is the CGI-I. And that facilitates the interpretation of what constitutes a meaningful within and between patient change in clinical outcome assessment. And so, this RSBQ AUC was born.

The additional advantage of this method is that we're able to capture clinically meaningful treatment effect and disease progression at the same time. The RSBQ AUC, which stands for area under the effect curve, the summary measure that combines both treatment effect and disease progression into one composite score. It captures not only the end of the treatment effect, but also the progression of the disease over the course of the study, with better precision than only an end-of-treatment score. And it's been published and demonstrated, as you can see the reference.

The CGI-I, clinical global impression of improvement anchored RSBQ AUC score, is now using the improvement threshold of at least 1 full point in the 7-point scale, which reaches from no change, which is a score of 4, to at least a score of minimally improved, which is a score of 3, or even higher to much improved, which is a score of 2, or very much improved, which is a score of 1. So the responder is now defined as a study participant who exceeds the clinically meaningful CGI-I threshold, with corresponding RSBQ AUC link value indicating clear improvement. Importantly, the CGI and RSBQ AUC has been previously successfully assessed as an efficacy endpoint in the US Rett syndrome trial RS-001.

I'd like to also now share more details about the CGI scale, because it's important in that context. The clinical global impression of improvement scale is a measure developed for use in clinical trials to provide a brief, standalone assessment of the clinician's view of the

patient's global functioning prior to and after initiating a study medication. Each time the patient is seen after the medication has been initiated, the clinician compares the patient's overall clinical condition to the period just prior to the initiation of medication use, which is the so-called baseline visit. That mimics what a physician would do in practice if an intervention is helping, and he could assess that. It measures both global and individual domain ratings, like CGI-S, which is the clinical global impression of severity, and the CGI-I measures clinical change in a very much worse, which is score 7, to very much improved, score 1 range.

The CGI-S score obtained at the baseline initiation visit serves as a good basis for making the assessment. The following question is rated on a 7-point scale, and the question is posed to the physician compared to the patient's condition at admission to the project, prior to medication initiation. This patient's condition is, 1, very much improved since initiation of treatment; 2, much improved; 3, minimally improved; 4, no change from baseline; and 5, minimally worse; 6, much worse; 7, very much worse since the initiation of treatment. So you can see that only the scores of 1 or 2 or 3 are defined as treatment responders, which is a very high bar. Score of 3 or less represent clearly observable clinically meaningful manifestation of drug effect. That implies that the minimal important difference is a change of one unit at least, which is from the CGI of 4 to a CGI of 3.

Let me now share briefly the ADAMS score, which is the Anxiety, Depression and Mood Scale. The Anxiety, Depression and Mood Scale, ADAMS, is the measure of anxiety and mood symptoms in individuals with intellectual disability. It has been clinically validated for use in Rett syndrome and in Fragile X syndrome. The ADAMS generates a total score in five subscale scores. It encompasses manic hyperactivity behavior, depressed mood, social avoidance, general anxiety, and obsessive compulsive behavior. So let me now share the key endpoints, and then I will hand over to Ed Hammond, Dr. Hammond, for continuing the slides of the other endpoints.

So very pleased to announce that the primary endpoint, which I just described, that ANAVEX 2-73 induces a clinically meaningful improvement of RSBQ AUC, which is the CGI anchored minimum required improvement for reaching a significant clinically meaningful improvement, with 72.2% of all patients in the study. That is a very meaningful score, as compared to 38.5% on placebo. What's also noticeable is that the Cohen's d effect size is very large, with 1.91 points.

Let me move to the secondary endpoints. The secondary efficacy endpoints, ADAMS and CGI-I, the left side, we see that the ADAMS score had a clinically meaningful and statistically significant reduction of emotional behavior symptoms response for ANAVEX 2-73 treated adult patients with Rett syndrome, of 52.9%, versus placebo of 8.3%. Also here there's a threshold. The threshold is defined by an improvement of at least 20 points change, 20% point change, which is an improvement of the ADAMS total score from baseline.

And on the right side, the CGI-I score, which demonstrated significantly more patients achieved clinically meaningful CGI-I response over the treatment duration in ANAVEX

2-73 treated group was 72.2% as compared to placebo of 38.5%, with also meaningful and significant p value. The Cohen's d effect size is also very large, with 1.91. So the threshold again was here, at least a minimal improved, if not much improved or very much improved. So now I'd like to hand over to Dr. Hammond to explore and explain the other endpoints. Please kindly proceed.

Edward R. Hammond
Thank you very much, Christopher. Hello, everybody. So we will now cover the other endpoints that were assessed in the AVATAR study, including here, the quality of life and seizures, and then in subsequent slides contextualized with biomarker assessments that were obtained during the study.

Beginning with quality of life assessed by the Child Health Questionnaire-Parent Form 50, the CHQ-PF50, this is an internationally recognized general health-related global measure of quality of life, and it encompasses physical and psychosocial concepts. These would include physical function, psychosocial behavior, bodily pain, emotional impact, family activities, family cohesion, and general health perceptions. ANAVEX 2-73 demonstrated dose-related significant improvement in overall quality of life as measured by the CHQ-PF50 total score, with a p value of 0.030.

To the right of this slide, what we display here is the frequency of seizures during the study period for ANAVEX 2-73 in blue, and for placebo in red. And you can observe that ANAVEX 2-73 reduces the frequency of seizures, and it was – treatment with ANAVEX 2-73 was associated with a 50.7 reduction in weekly seizure risk.

Next slide, please. So the AVATAR Rett syndrome clinical trial evaluated potential biomarkers of clinical response. There is evidence that a use of biomarkers in drug development increases the chances of success through early stages of development or through to new drug or to biologic license application filing. Biomarkers in drug development will set the stage for consistency and for reproducibility of trial findings, by reducing the variability in trial participant and also for endpoint selection. And this is one of the reasons why we sought to develop biomarkers for our program as well.

Next slide, please. Here's an overview of the ANAVEX 2-73 mechanism of action, which we have covered at the beginning of this presentation, but here in reference to Rett syndrome. So the MECP2 mutation leading to Rett syndrome induces alteration of synaptic development and drives chronic cellular stress by unraveling chromatin. The ensuing mitochondrial dysfunction and increased inflammation contributes to the symptoms that are expressed in persons with Rett syndrome.

Of important mention is a decrease in GABA in patients who have Rett syndrome. GABA is an inhibitory neurotransmitter, and in the brain has anti-seizure and anti-anxiety effects, which leaves persons with Rett syndrome prone to seizures and mood disorders. L-alpha-aminoadipic acid, L-AAA, has also been shown to be increased in persons with Rett syndrome. L-AAA is involved in the neuroligin pathway and involved in excitatory neurotransmission, as well as in neurodegenerative processes and diseases. ANAVEX 2-

73 reverses these behavioral, motor and synaptic imbalances by activation of the SIGMAR1.

On to next slide, please. So we will now speak of GABA as a potential biomarker, predicting clinical outcome in ANAVEX 2-73 Rett syndrome study. In patients with Rett syndrome, the MECP2 deficiency disrupts this GABAergic cycle, resulting in decreased GABA, and impairs synaptic and mitochondrial function. The AVATAR efficacy endpoint demonstrated statistically significant and clinically meaningful reductions in Rett syndrome's symptoms, and these were related to changes in potential biomarkers of disease pathology.

GABA was significantly increased at p of 0.0205. The gliotoxin, L-alpha-aminoadipic acid, L-AAA, was significantly decreased with a p value of 0.0392. These changes in biomarkers taken together are supportive and contextualize the findings of decreased seizure frequency, improved health-related quality of life, and behavioral measures that were observed in the AVATAR trial. So now what we'll cover here then are safety and adverse events that occurred during the treatment period.

ANAVEX 2-73 was well-tolerated with very good medication compliance of 95%. We observed similar treatment, emergent adverse events, TEAEs, in the ANAVEX 2-73 treated persons and the placebo arms. Adverse events at the 10% threshold or more were predominantly mild or moderate. The 10% threshold translates the occurrence of two or more events and is set because of this small sample size where one event was over 7%.

No clinically significant changes in vital signs, laboratory values, ECG parameters were observed in the ANAVEX 2-73 or the placebo groups. There was no incidence of diarrhea or vomiting. These safety findings are indeed consistent with a known safety profile of ANAVEX 2-73. I will hand over back to you, Dr. Missling.

Christopher U. Missling
Thank you very much, Dr. Hammond. So overall, in summary, we can confirm that the Phase 3 AVATAR clinical trial for adult patients with Rett syndrome accomplished the primary efficacy endpoint of RSBQ AUC, the secondary efficacy endpoints of ADAMS and CGI-I, all statistically significant, as well as safety endpoints were met.

The efficacy endpoints were statistically significant and clinically meaningful in Rett syndrome symptoms with related changes in potential biomarkers of disease pathology. Thereof, GABA was significantly increased, which is decreased in Rett syndrome patients; and L-AAA was significantly decreased, which is usually increased in Rett syndrome patients.

We have a convenient once-daily oral liquid formulation, which was well-tolerated up to 30 milligram per day without safety concerns identified. We also confirmed a dose response. The RS-001 study used 5 milligram as you know, and the RSBQ AUC Cohen's d effect size was 0.517. and the RS-002 AVATAR study with higher dose, 30 milligrams was by a magnitude higher and reached the effect size of 1.91.

The analysis of weekly seizure counts indicated that relative to placebo, ANAVEX 2-73 is associated with a 50.7% reduction in weekly seizure risk. And ANAVEX 2-73 demonstrated dose-related significant improvements in the overall quality of life, which is measured with the CHQ-PF50 and a p value of 0.030, which is very important for discussion of the pricing with insurance companies. And the key milestone was meant to advance regulatory approval pathway for the adult patients with Rett syndrome. As a matter of fact, we are now in discussion – discussing with the FDA a pathway for potential approval of ANAVEX 2-73 for adult patients with Rett syndrome.

I'd like to acknowledge and thank all of the patients and their family members who participated in the Rett syndrome study, as well as the investigators and their staff conducting these studies, and the global Rett Syndrome Association. And last but not least, also the team at ANAVEX, which worked very hard to execute this trial.

In summary, we'd also like to finish with an overview of the ANAVEX pipeline, which now has reached even a stronger foothold as a platform for targeting neurodegenerative diseases, including Alzheimer's and Parkinson, as well as neurodevelopmental diseases, which now includes the franchise of Rett syndrome, but also other autism spectrum related disorder, which are infantile spasms, Fragile X, Angelman syndrome, and other related disorders.

So in summary, we believe ANAVEX is at this point the only company pursuing the large markets with application of precision medicine, with confirmed biomarker response, to develop treatment for both global aging, which includes CNS, Alzheimer's and Parkinson's disease, as well as catastrophic orphan genetically caused diseases like Rett syndrome, with high unmet need. We found and confirmed the platform with the AVATAR study today, and we identified even further biomarkers of pathology responding to the drug effect, which as we know improves the chance of clinical success and makes the data more robust.

We also have strong IP position around our novel mechanism of action of ANAVEX 2-73, with composition of matter up to at least 2037. And we have now a compelling human data platform, which includes the Phase 3 AVATAR study in Rett syndrome, the Phase 2 Rett syndrome study, and the Phase 2 study in Parkinson's disease dementia, PDD, and a Phase 2a study in ANAVEX in Alzheimer's disease, with favorable and exploratory efficacy results through 148 weeks.

And we also like to mention, last one but not least, we're expecting the Phase 2/3 ANAVEX 2-73-AD-004 Alzheimer's study to readout on time in the second half of this year.
With that, I'd like to go back – get back to Clint for Q&A. Thank you.

Q&A

Clint Tomlinson

Thank you, Christopher. We'll now begin the question-and-answer session. If you have a question, please raise your hand or enter it in the Q&A box. The first question is coming from Charles Duncan from Cantor Fitzgerald.

Charles C. Duncan Q
Yeah. Hi. Can you hear me?

Clint Tomlinson A
Yeah. We're good.

Charles C. Duncan Q
Okay. Super. Good morning. Yeah, thanks for taking the question. And Christopher, congratulations on these provocative results in a very high unmet need patient population. I had a couple of questions on the trial conduct, and then I wanted to ask you about next steps. With regard to the sample, I guess I'm kind of wondering if you can help me understand why the sample numbers are imbalanced between control and experimental arms, 20 versus 13, I guess, in the reverse order?

And then if you could help us understand a little bit more about the titration paradigm, and then the number of patients that were a little bit higher weight on the control arm. I guess I'm wondering if any of these factors may have played into the results. And then I'll ask you about the endpoint question that I wanted to ask.

Christopher U. Missling A
Right. So let me start first with the last question, the weight. We have done extensive analysis, the drug does not depend on weight of a participant. It's weight independent. So we believe that does not have any effect. Regarding the imbalance of the active arm being randomized 3:2, it was the wish of the community to have at least as possible exposure to placebo in a trial, given that these patients are highly vulnerable, hard to find, and not easy to be convinced to participate in a study. So that was the reason why we have that 3:2 randomization, basically favoring slightly higher number of active arm and placebo arm.

Charles C. Duncan Q
Okay. That makes sense. And then regarding the titration, how did it actually work? What was the percentage of patients that got to that 30-milligram dose? And can you give us a sense of how that progressed over, call it the seven-week trial? What was the exposure, I guess, response that you were looking for?

Christopher U. Missling A
So almost all patients reached the 30-milligram dose, I think it was 80%. And some patients were, because the seven weeks relatively was a flat titration, didn't get fully there. But you can definitely say that the totality of the data is based on the average of slightly short of 30 milligram.

Charles C. Duncan Q

Okay. And then relative to or regarding the endpoint, I guess I'm really intrigued with the anchor-based endpoint analysis, and I like it in some ways. But I also kind of wonder if, I mean, didn't the trial start off within RSBQ total? And isn't that the endpoint in the ongoing EXCELLENCE trial? And I guess I'm wondering if you also looked at the data with regard to a change in RSBQ relative to baseline. And then the other thing I wanted to ask, which I'm confused on, is it looks like the CGI data is exactly the same as the primary endpoint data. And I'm wondering if I'm just confused in seeing that.

Christopher U. Missling A
Yeah, good point. So let me also get – address the second part. So the CGI-I response is indeed numerically similar or same as the RSBQ response, but it's coincidental. It's not the same in its patients' response.

Charles C. Duncan Q
Okay.

Christopher U. Missling A
The RSBQ total score is actually – and we had included that in our analysis, and we basically did not change the – or the CRO didn't change on time, in the ClinicalTrials.gov that's why it looks like it was changed. But it was actually pre-specified. In a Phase 3 you cannot really move around with the endpoint, so it was pre-specified. As I mentioned, we also included that in the RS-001 and we also showed it in our slides, but we didn't highlight that that analysis. But the discussion with FDA led to a conviction that the RSBQ alone is not sufficient as a standalone to measure because of its likely type 1 and type 2 error potential. So the anchor-based correlated threshold based RSBQ was then chosen, which is the RSBQ AUC.

Again, I want to make sure everybody understands that is a much higher threshold, because if you have just the average improvement of a very small percentage or a very small effect of the RSBQ, for example, you are not helping the patient. You might have a significant signal, but it's not helping the patient. What we have is a much more rigorous threshold you'd have to overcome, and then you start looking at the RSBQ. So that is much a higher hurdle and much more difficult to accomplish.

The analogies to a trial, for example in psoriasis, where this also performed such analysis, you have to have a minimum of 75% of removal of the area of the arm or the body part where psoriasis is affected. And it's not just 5% on average improvement over placebo, it has to be at least 75%. And then from that moment on, you count as a responder. So the threshold is much higher in the calculation, and that's what is actually on our end here, an accomplishment because we had to adhere to this more rigorous approach.

Charles C. Duncan Q
That makes sense to me. And I assume the clinician is blinded to the treatment randomization arm when doing the assessment of CGI?

Christopher U. Missling A

Absolutely. It's four times blinded. The participant, the patient, we and the assessment and the CRO. So everybody is blinded.

Charles C. Duncan Q
Okay. Last question. Sorry for all of them, but I promise it's last. Next steps regarding meeting with the agency, I assume you don't know the exact timing, but could you give us kind of a goal on that? And then would you be discussing a second Phase 3 to replicate these results? Or would you rely on EXCELLENCE and the body of data that you have thus far to potentially support the filing of an NDA?

Christopher U. Missling A
Yeah. I mean, it's not unheard of. We've seen it with the approval of the vaccines for COVID, that it was first tested in adults and it was then approved for adults, and then it was tested in younger children, and then it was approved in younger children, and now the age group was expanded further. So we don't want to exclude the ability now with this data package to seek approval for retinue for adult patients. On the other hand, we'd like to have the discussion with FDA first, because we also have the, as you know, EXCELLENCE study ongoing which includes patients 5 to 17. So regarding timing, I would like to say at this point in time, as soon as we can. So we'd like to able to move forward the discussion as soon as possible.

Charles C. Duncan Q
Thank you.

Christopher U. Missling A
Thank you.

Clint Tomlinson A
Thank you, Charles. The next question comes from Soumit Roy from Jones Research. Soumit, you can go ahead when you're ready. Soumit, are you there?

Soumit Roy Q
Hi. Can you hear me?

Clint Tomlinson A
Yeah. Soumit, go ahead. Go ahead, please.

Soumit Roy Q
Apologies for that. So one question, I guess we are getting a bunch of questions from the investors, is going back to the endpoint. When – we were not – when was the switch happened, we weren't really sure of RSBQ score to AUC, but I guess the bigger question is what is the delta between the baseline in the treatment arm and the placebo arm and the RSBQ score? If you can give us a number or at least qualitatively tell us if it's more than 14.5 we saw in the previous, or less? Any color would be appreciated?

Christopher U. Missling A

Yeah, absolutely. So we had – the 14.5 came from the wild type in all patients in the US Rett study. So the total includes also patients without the wild type. So we definitely can say comfortably that the correlation is from the – with the threshold, the bar of one point CGI-I score, that it must be in the range of above 10 to 29 in that range. So 10 to 29 in that range is the likely range of the RSBQ response.

Soumit Roy Q
Got it. And the seven-week exposure, do you believe a longer drug exposure could further improve it, or this is somewhere you have seen this maxes out? Any thoughts around that?

Christopher U. Missling A
Right. It's an excellent question. So we have now expanded the study in extension, and we had some patients not getting the drug extension right away. So we will be able to see in a fresh new baseline how these patients progress, which were also on study drug prior and were on placebo prior. So we will have data on that upcoming to see if the effect of the drug requires longer duration of drug, or the 7-week is sufficient. We believe the 7-week is sufficient. It will be something which we will explore and find out.

Soumit Roy Q
Perfect. And just the last question, have you done the analysis like previous Phase 1 trial percent to responders versus non-responders yet?

Christopher U. Missling A
Yes. As I said, we should go all and look back up in the presentation of the ANAVEX presentation corporate slide deck, which is included in, and let me look it up the slide where we have it shown, the respond analysis. So it's not that we didn't it for the first time, but we just did not highlight it. So it was like probably not noticed as much as now, since this is the requirement for the Phase 3, which is a much more rigorous threshold to be able to accomplish. So slide 22 in the ANAVEX global corporate presentation, you see the respond analysis of the CGI-I, the ADAMS, the RSBQ, CGI-I and the ADAMS as well.

Soumit Roy Q
Thank you so much and congratulations again.

Christopher U. Missling A
Thank you.

Clint Tomlinson A
Thank you, Soumit. The next question is coming from Yun Zhong from BTIG.

Yun Zhong Q
Hi. Thanks very much for taking the question. So one question, follow-up question on the endpoint, I assume that when you report top-line data from the EXCELLENCE study, it will be RSBQ AUC as well. Do you have to go back to the US Phase 2 study to reanalyze the data using AUC versus the – as compared to the original RSBQ to make everything consistent?

Christopher U. Missling A
Good question. Thank you. So that's right, the EXCELLENCE study will use the same endpoint because as just described, it is just the preference of the FDA. Regarding going back to redo the analysis, it's not actually necessary. It's already out there. It's already included in slide 22 of the presentation. We just did not provide the fine points of the threshold levels in those slides, but we pointed out. And I see here on the bullet in the bottom of the slide 22, the slide, we said respond analysis is capturing the progression of the disease and treatment effect over the course of the disease and the improvement in the adults required meaningful according to published criteria. So we basically have already analyzed that; it's the same analysis which we applied here, which was already done prior. We just didn't highlight the exact method in the US study, but it was exactly done the same way. And the data is actually on slide 22.

Yun Zhong Q
Okay. And now that we know the dose used in the AVATAR study, are you able to disclose the dose being tested in the pediatric study?

Christopher U. Missling A
Yeah. I would say at this point in time, it's in the ballpark of the dose of the AVATAR study.

Yun Zhong Q
Okay. And another question is on the biomarker, very interesting biomarker data. But if I remember correctly, from the US Phase 2 study, you initially saw a very interesting biomarker, glutamate and GABA. But then from the entire study, the signal seems to have disappeared. So are you worried that the biomarker truly is reflecting what's going on? And also, have you looked at the – any correlation between biomarker response and clinical response as you did before?

Christopher U. Missling A
No. We are now doing the analysis of the biomarker response correlation, as well as what I pointed out at the beginning, we have not yet the data of the SIGMAR1 mRNA, which was a very strong correlation of the effect of the drug with the SIGMAR1 expression in correlating very nicely with the endpoints. The question about the glutamate and GABA, they are interrelated. And I like to point out, we only had showed in the open-label study preceding the US study, which was a six patients open label, we had some weak signal of glutamate reduction, which is considered positive. The glutamate is too much elevated in the Rett syndrome. But in the AVATAR study, we didn't see that strong enough. But the GABA was strong enough, which is basically the opposite. We have to also appreciate that these measures from the blood are sometimes not perfect, and they just also have their own variability.

But the fact that the GABA was increased is really important because we had a higher – we didn't see that in the US study, which we believe is based on the fact that the US study was lower in dose. So it might be that you need to have a higher dose to push through to

see the biomarker effect. And we saw that in the AVATAR study, as well as the other biomarker measure, which was the L-AAA, which was decreased which usually is too high. So I think that's kind of like a strong picture.

Yun Zhong Q
Okay, so last question. Are we able to see any additional data from the study before maybe mid-year when you report pediatric side data?

Christopher U. Missling A
Yes, we expect more data. as I mentioned, the mRNA and additional biomarker data, as well as what I referred to before, the analysis of the patients, which were on the prior study and then switching to the extension study, what happen to them. And also, I'd like to point out at this occasion here that all these biomarker effects, the GABA increase and the L-AAA decrease, are all applicable to diseases beyond Rett syndrome. So we have the same pathology of biological negative loop or imbalances in the pathology of other autism spectrum disorders like Fragile X, but also in Parkinson and in Alzheimer's disease. So these biomarkers actually are quite important indications, potentially for the effect also of the other indications which we are pursuing right now.

Yun Zhong Q
Okay. Thank you very much and congratulations.

Christopher U. Missling A
Thank you.

Clint Tomlinson
Thank you, Yun. So I don't see any further questions at this time, Dr. Missling.

Christopher U. Missling
Thank you. So we're very excited and thank you for joining us. We're very excited to have reached this milestone and expect to continue our momentum, including the release of the upcoming Phase 2/3 EXCELLENCE ANAVEX 2-73 clinical trial in pediatric Rett patients, as well as the Phase 2b/3 in ANAVEX 2 -73 in Alzheimer's patients. And we will look ahead and we continue to focus on driving meaningful growth across our broad SIGMAR1 receptor platform portfolio, to deliver transformational treatments for patients with both degenerative and developmental neurologic disorders around the world. We look forward to providing you further updates as advancements continue. Thank you very much.

Clint Tomlinson
Thank you, ladies and gentlemen. This concludes today's conference call. Thank you for participating. You may now disconnect.